REMARKS

Claims 1, 4-10, and 14-24 are pending in this application. Claims 10, 14-18, 20, and 24 are rejected under 35 U.S.C. § 112, first and second paragraphs. Claims 1, 4-8, 10, 14, 15, 17, 18, and 20-24 are rejected under U.S.C. § 103(a). Claims 1, 4, 6-8, 10, 14, 17, 18, 20, 23, and 24 are provisionally rejected under the doctrine of non-statutory obviousness-type double patenting. Claims 9 and 19 are withdrawn from consideration due to a restriction requirement. Each of these rejections is addressed below.

Claim Amendments

Claim 1 has been amended to require the second polypeptide to contain the extracellular region of granulocyte colony stimulating factor ("G-CSF") receptor and the cytoplasmic region of c-mpl. This amendment finds support, for example, at page 31, lines 19-24, of the specification and in Figure 20. Claim 10 has been amended to recite that the desired exogenous gene and the DNA encoding a fusion protein are located on the same molecule. Support for this amendment may be found, for example, at page 7, line 26, to page 8, line 2, and page 8, lines 8-18, of the specification. In view of the amendment to claim 10, the language of claims 22 and 24 has also been amended.

New claims 25 and 26 have been added. Claim 25 finds support, for example, at page 5, lines 21-25, page 6, lines 24-26, and page 8, lines 2-7, of the specification, and claim 26 finds support, for example, at page 5, lines 21-25, and page 8, lines 2-7, of the

specification.

Claims 9, 16, 17, 19, and 21 have been canceled. The present amendments were made solely to expedite prosecution. Applicants reserve the right to pursue canceled subject matter in this or in a continuing application. No new matter has been added by the present amendments.

Rejection under 35 U.S.C. § 112, First Paragraph

Claims 10, 14-18, 20, and 24 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement based on the assertion that the claims contain new matter. In particular, the Office states (page 4):

> [T]he specification as originally filed lacks support for "a vector" comprising multiple molecules.

Applicants submit that claim 10 and its dependent claims, as amended, are free of this basis for rejection.

Rejection under 35 U.S.C. § 112, Second Paragraph

Claims 10, 14-18, 20, and 24 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. The Office asserts that "[t]he term vector, as used in the art and in the instant specification, refers to a single vector molecule." Applicants submit that the claims, as amended, are free of the § 112, second paragraph rejection.

Rejection under 35 U.S.C. § 103

Claims 1, 4, 6-8, 20, and 23 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Gurney et al. (Proc. Natl. Acad. Sci. USA 92:5292-5296, 1995; "Gurney") in view of Jackson et al. (EMBO J. 12:2809-2819, 1993; "Jackson"). Claim 1, has been amended to incorporate the limitations of claim 22, which was deemed free of this rejection.

Claims 1, 4-8, 10, 14, 15, 17, 18, and 20-24 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Ito et al. (Blood 90:3884-3892, 1997; "Ito") in view of Gurney. Claims 17 and 21 have been canceled and the rejection of these claims is moot. Applicants address this basis for rejection as it applies to the present claims as follows.

Where "claimed subject matter has been rejected as obvious in view of a combination of references, a proper analysis under § 103 requires, *inter alia*, consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should . . . carry out the claimed process; and (2) whether the prior art would have revealed that in so . . . carrying out, those of ordinary skill would have a reasonable expectation of success." *In re Vaeck*, 947 F.2d 488, 493, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991). "Both the suggestion and the expectation of success must be founded in the prior art, not in the applicant's disclosure." *In re Dow Chem. Co.*, 837 F.2d 469, 473, 5 U.S.P.Q.2d 1529, 1531 (Fed. Cir. 1988). As the Federal Circuit has observed (emphasis added):

> A critical step in analyzing the patentability of claims pursuant to section 103(a) is *casting the mind back to the time of invention*, to consider the thinking of one of ordinary skill in the art, guided only by the prior art references and the then-accepted wisdom in the field. . . . *Most if not all inventions arise from a combination of old elements*. . . . Thus, every element of a claimed invention may often be found in the prior art. . . . However, identification in the prior art of each individual part claimed is insufficient to defeat patentability of the whole claimed invention. . . . Rather, to establish obviousness based on a combination of the elements disclosed in the prior art, there must be some motivation, suggestion or teaching of the desirability of making the specific combination that was made by the applicant.

In re Kotzab, 217 F.3d 1365, 1369-70, 55 U.S.P.Q.2d 1313, 1316 (Fed. Cir. 2000) (citations omitted) (emphasis added).

Applicants submit that the cited art fails to provide a motivation, suggestion or teaching of the desirability of making the fusion protein of claim 1, as amended, and the vector of claim 10, as amended.

Claim 1

Claim 1 has been amended to be directed to a fusion protein containing a first polypeptide including a ligand-binding domain of a steroid hormone receptor that, upon ligand binding, dimerizes, and a second polypeptide containing the extracellular region of a G-CSF receptor and the cytoplasmic region of c-mpl or a proliferation inducing part thereof that, upon said dimerization of said first polypeptide, imparts proliferation activity to a cell. Neither Ito nor Gurney, alone or in combination, provides any motivation to make a fusion protein containing all of the features required by claim 1.

Gurney fails to teach or suggest not only the desirability of combining a ligand-binding domain of a steroid hormone receptor with the cytoplasmic region of c-mpl, or a proliferation inducing part thereof, in a fusion protein, but also fails to provide a reason, suggestion, or motivation to generate a fusion protein that further contains the extracellular region of a G-CSF receptor as presently claimed.

Applicants note that Ito fails to describe c-mpl. Ito also fails to provide a motivation to make the specific combination of elements contained in the claimed fusion protein and provides no suggestion or motivation to combine its teachings with those of Gurney. Nothing in Ito would motivate one skilled in the art to engineer a fusion protein that contains (i) a ligand-binding domain of a steroid hormone receptor, (ii) the cytoplasmic region of c-mpl, or a proliferation inducing part thereof, and (iii) the extracellular region of a G-CSF receptor. Applicants submit that the obviousness rejection of claim 1, as amended, and its dependent claims, should be withdrawn.

In short, Gurney and Ito, alone or in combination, do not render the invention of claim 1 obvious. The U.S.C. § 103 of claim 1, as amended, and its dependent claims should be withdrawn.

Claim 10

Claim 10 and its dependent claims, as amended, are directed to a vector that includes a desired exogenous gene and a DNA encoding a fusion protein and require that

the desired exogenous gene and the DNA encoding the fusion protein are located on the same molecule. In addition, the claims require the fusion protein to contain a ligand-binding domain of a steroid hormone receptor and a c-mpl, or a proliferation inducing part thereof. The present amendments incorporate the features of claim 16 (now canceled), which was deemed free of this rejection, into claim 10. Applicants submit that claim 10, as amended, is non-obvious over the cited art. Nonetheless, for the sake of completeness, Applicants note that the cited art fails to provide a motivation, suggestion or teaching of the desirability of making the claimed vector.

Gurney fails to teach or suggest a single vector containing both an exogenous gene and a DNA encoding a fusion protein including a ligand-binding domain of a steroid hormone receptor and a c-mpl. Nothing in Gurney suggests that a desired exogenous gene and a gene containing fusion protein could be contained on a single vector or that it would be desirable to do so.

Moreover, as noted in Applicants' last reply, Gurney fails to teach or suggest the desirability of combining a ligand-binding domain of a steroid hormone receptor with c-mpl. Gurney describes chimeric receptors,containing the extracellular domain of the human growth hormone receptor and the intracellular domain of c-Mpl. Growth hormone receptors and steroid hormone receptors have substantially different structures as well as divergent ligand binding and signal transduction mechanisms. Given the disparity between the structure and function of growth hormone receptors and steroid hormone

receptors, Applicants submit that Gurney fails to teach or suggest the desirability of making a fusion protein containing a ligand-binding domain of a steroid hormone receptor and c-mpl, much less a single vector containing a DNA encoding such a fusion protein as well as a desirable exogenous gene.

Ito describes vectors containing a DNA encoding a fusion protein including a granulocyte colony stimulating factor receptor and the hormone-binding domain of an estrogen receptor; Ito fails to describe c-mpl. As such, Ito fails to teach or suggest the invention of claim 10, as amended. Ito also fails to provide any motivation to combine its teachings with those of Gurney. In fact, Ito states (page 3891):

> We are also constructing similar chimeric genes using other growth factor receptor genes such as *c-kit* and erythropoietin receptor genes. However, the G-CSFR [granulocyte colony stimulating factor receptor] gene may be the most appropriate for clinical application, since it has already been extensively studied and, more importantly, there is plenty of experience in the clinical use of rhG-CSF [recombinant human granulocyte colony stimulating factor]. The safe use of rhG-CSF in humans suggests that the signals from exogenously expressed G-CSFR-derived molecules <u>are safer than those of other receptors</u>. (Emphasis added.)

Thus, Ito indicates that the safe use of rhG-CSF in humans suggests that signals from G-CSFR-derived molecules are safer than those of other receptors. In view of this statement, one skilled in the art would not have been motivated to substitute c-mpl, taught by Gurney, for G-CSFR in a fusion protein containing a ligand-binding domain of a steroid hormone receptor.

In particular, claim 10 requires the c-mpl portion, upon dimerization of the portion

containing the ligand-binding domain of the steroid hormone receptor, to impart proliferation activity to a cell (i.e., to be a signal transducing portion). Ito, while mentioning possible chimeras containing other growth factor receptor (*c-kit* or erythropoietin receptor) portions, clearly teaches away from the desirability of making vector expressing a chimera with a signal transducing portion other than a portion from G-CSFR. Applicants note that a *prima facie* case of obviousness cannot be maintained where the prior art teaches away from the claimed invention. As the Federal Circuit recently reiterated in reversing a Board decision finding obviousness:

> A prima facie case of obviousness can be rebutted if the applicant ... can show 'that the art in any material respect taught away' from the claimed invention .... *A reference may be said to teach away when a person of ordinary skill, upon reading the reference, ... would be led in a direction divergent from the path that was taken by the applicant.*

In re Haruna, 249 F.3d 1327, 1335, 58 U.S.P.Q.2d 1517, 1522 (Fed. Cir. 2001) (emphasis added) (citations omitted).

Applicants submit that the expressed preference by Ito for G-CSFR as the signal transducing portion of a fusion protein would not have led one skilled in the art to substitute a sequence encoding a signal transducing G-CSFR portion of a fusion protein with a sequence encoding a c-mpl portion to impart proliferation activity to a cell. As such, Ito teaches away from making a vector encoding a fusion protein recited in claim 10.

For all the above reasons, neither Gurney nor Ito, alone or in combination renders

the invention encompassed by claims 10, as amended, and its dependent claims, obvious. This basis for rejection should be withdrawn.

Double Patenting

Claims 1, 4, and 23 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 3, and 4 of co-pending application number 09/142,305 in view of Solar et al. (Blood 92:4-10, 1998; "Solar"). Claim 1 has been amended to incorporate the limitations of claim 22. In view of the present amendment, Applicants submit that this basis for rejection should be withdrawn.

Claims 6-8, 10, 14, 17, 18, 20, and 24 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatenable over claims 8, 12, 14, 15, 17, and 18 of co-pending application number 09/905,592 ("the '592 application") in view of Gurney[1]. Applicants submit that, in view of the present amendments to claims 1 and 10, this basis for rejection should be withdrawn.

[1] The Office Action at first lists claims 6-8, 10, 14, 17, 18, 20, and 24 as being provisionally rejected on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 1,3, and 4 of the co-pending '592 application in view of Solar, but the Office's arguments appear to be directed to claims 8, 12, 14, 15, 17, and 18 of the '592 application and Gurney.

CONCLUSION

Applicants submit that the application is in condition of allowance, and this action is hereby respectfully requested. Nonetheless, if there are any remaining issues, Applicants respectfully request a teleconference with the Examiner to bring this case into condition for allowance.

Enclosed is a petition to extend the period for replying to the Office Action for three months, to and including May 30, 2006, as May 29th is a federal holiday, and a check in payment of the required extension fee.

If there are any additional charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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